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*Dedicated to Full Member of the Russian Academy of Sciences I.P. Beletskaya on her jubilee*

# Metallomicellar Complex of 1-Hexadecyl-4-aza-1-azoniabicyclo-[2.2.2]octane Bromide with Copper Dibromide for Solubilization of Nitrofurantoin

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**Abstract**—Associates of amphiphilic 1-hexadecyl-4-aza-1-azoniabicyclo[2.2.2]octane bromide–copper dibromide complex solubilize nitrofurantoin (furadonin). The solubilizing capacity of premicellar aggregates with respect to nitrofurantoin is 15 times higher than that of micelles and is considerably higher (by a factor of 5–16) than the solubilizing effect of micellar solutions of the complex, ligand, and conventional cationic surfactants with respect to Orange OT.

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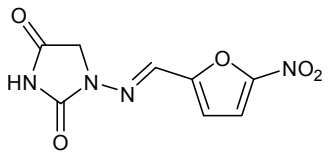
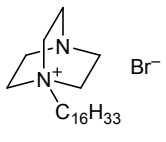
The synthesis of surfactants containing transition metal atoms (metallosurfactants) and study of their properties in solution constitute an important research line in the field of supramolecular chemistry and design of biomimetic compositions [1–3]. Numerous examples of using metallosurfactants in the catalysis of biochemical processes [2, 3], colloidal syntheses of nanoparticles [1], manufacture of mesoporous materials [4], magnetic resonance imaging [5, 6], etc., have been reported. An important characteristic of metallomicellar systems determining the possibility of their practical application (including catalysis of chemical processes and solution of environmental and medical problems) is their increased ability to solubilize substances that are poorly soluble in working medium [4]. We are conducting research on the effect of micellar solutions, including those based on metallosurfactants, on the solubility of drugs [7–9]. Herein we report the results of our study on the effect of metallomicelles on the solubility of nitrofurantoin which is an antimicrobial drug widely used in medical and preventive practice. Nitrofurantoin (**1**, 1-{(*E*)-[(5-nitrofuran-2-yl)-methylidene]amino}imidazolidine-2,4-dione) is a yellow or orange–yellow crystalline powder almost insoluble in water and ethanol. Its solubility in water at 24°C is 79.5 mg/L [10].




**1**




**2**

In order to improve the solubility of **1** in water and thus increase its bioavailability, we propose to use micellar solutions of the 1:1 complex formed by a cationic surfactant with a bicyclic head group, 1-hexadecyl-4-aza-1-azoniabicyclo[2.2.2]octane bromide (**2**, D-16), and copper dibromide (**2**·$CuBr_2$). As we showed previously, this metallosurfactant is characterized by a high aggregation activity. The critical micelle concentration (CMC) of the complex at 25°C determined by tensiometry and conductometry is 0.65 and 0.61 mM, respectively [11]; these values approach or even slightly lower than CMCs of known analogs with cyclic and acyclic head groups, cetylpyridinium bromide (0.68 mM, 25°C, tensiometry